REMARKS

I. Status of the claims

Claims 1-22, 24, 26-29, 32-53, 55, 57-60, and 63-82 are pending. Claims 23, 25, 30, 31, 54, 56, 61, and 62 have been canceled. Claims 63-80 have been withdrawn. Claims 1, 11, 13, 26, 32, 42, 57, and 58 have been amended for the reasons that follow below. In short, claim 1 has been amended to recite a "core carrier" onto which the first and second nucleic acids are coated and a promoter that is active in a mammalian cell. The "core carrier" element is supported by page 17, lines 11-14 and page 39, lines 11-12. The mammalian promoter is supported by the specification at page 24, line 10. Other amendments have been made solely for grammatical purposes.

Claims 81 and 82 have been added to qualify the core carrier of claims 1 and 32 as made of gold, tungsten, platinum, iridium, ferrite, polystyrene, or latex. Support for this subject matter can be found at page 17, lines 11-14 and page 39, lines 11-12 of the original specification.

II. Drawings

The Examiner notes that "each page of the figures is labeled twice [*e.g.*, "1-2" and "2/23"], both labels are not mentioned in the Brief Description of the drawings." Office Action at page 2.

Applicants have amended the Brief Description of the Drawings to appropriately cite the correct figure identifier. Applicants point out that "2/23" reflects page 2 of 23 pages of figures. Applicants also have submitted herewith replacement sheets with the respective page designations deleted. Each figure is now denoted as described in the application and each page of figures is identified with a drawing label.

III. Sequence Letter

The Examiner notes that claims 13 and 32 "must be amended to recite SEQ ID Nos for KDEL and RDEL to be in sequence compliance." Office Action at page 2. Accordingly, Applicants have amended claims 13 and 32 appropriately by assigning SEQ ID NO. 27 to "KDEL" and SEQ ID NO. 28 to "RDEL." Applicants have submitted herewith a revised version of the Sequence Listing filed with the original application and received by the Office on November 26, 2001. The new Listing includes the appropriate identifier information under PatentIn v. 3.1 for SEQ ID NOs. 27 and 28.

IV. Claim objections

Claim 1

The Examiner states that "peptide" recited in claim 1 lacks antecedent basis. Applicants have amended claim 1 accordingly by reciting a "subunit **peptide**." Applicants also have amended claim 32 in similar fashion for the sake of consistency.

Claims 23 and 54

Purely for the purpose of expediting prosecution, Applicants have canceled claims 23 and 54 and therefore the objections raised by the Examiner [the claims do not allegedly further limit the preceding claims and an intended use is not appropriate] do not apply. Accordingly, Applicants believe that these rejections are now moot.

Claims 13 and 32-62

The Examiner states that the phrases "mature subunit peptide" and "C-terminal KDEL or RDEL motif in the subunit peptide encoded thereby" recited in claims 32-62 and 13 respectively, lack antecedent basis. Office Action at page 3.

Applicants have amended claim 32 to clarify that the subunit peptides *lack* either KDEL or RDEL.

V. Claim rejections under 35 U.S.C. § 112, 2nd paragraph

The Examiner states that claims 11 and 42 "set forth a combination of claim limitations that are not clear" because, according to the Examiner, "the recited modifications of any portion of the B subunit coding region would not result in a detoxified B subunit." Office Action at page 4. The Examiner states that "modifications of the A subunit would or could result in detoxification of the encoded subunit." Office Action at page 4.

To expedite prosecution, therefore, Applicants have amended claims 11 and 42 to recite that it is the A subunit that has been detoxified. Accordingly, Applicants respectfully request that this rejection be withdrawn.

VI. Claim rejections under 35 U.S.C. § 102

i. U.S. Patent No. 6,395,964 does not teach a promoter that is active in mammalian cells and, therefore, the present claims are not anticipated

Claims 1-10, 13-41, and 44-62 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Arntzen *et al.* (U.S. Patent No. 6,395,964).

The Examiner states that "Arntzen *et al.* disclose the instantly claimed invention directed to compositions that comprise first and second nucleic acid sequences" that encode truncated subunits A and B from ADP-ribosylating exotoxin, neither of which has an amino terminal bacterial signal peptide. Office Action at pages 4 and 5.

Applicants contend that the subject matter of the present claims is not anticipated by Arntzen *et al.* because none of Arntzen's constructs include promoters that are active and induce expression of an operably linked polynucleotide *in mammalian cells*. Arntzen *et al.* is concerned only with the use of transgenic plants as oral vaccines and not the introduction of nucleic acid constructs into mammalian cells. See, for instance, column 1, lines 10 to 37. The constructs in Arntzen *et al.* therefore use promoters that are operable in plant cells, *not* mammalian cells. The figures of Arntzen confirm that this is so. Those figures depict the constructs that employ plant promoters and in particular:

(i) the cauliflower mosaic virus 35S promoter (Fig. 1C and col. 7, lines 49 to 52);

(ii) the potato patatin promoter (Fig. 1A and col. 7, lines 52 to 59);

(iii) the *Agrobacterium* nopaline synthase promoter (Fig. 1A-C and col. 47, lines 49 and 50); and

(iv) the soybean vegetative storage protein B promoter (see Fig. 7 and col. 19, lines 38 to 41).

As all of the promoters employed in Arntzen are only operable in plant cells, Arntzen does not teach each and every element of claim 1. Accordingly, Arntzen does not anticipate the subject matter of claims 1-10, 13-41, and 44-62, and Applicants therefore respectfully request that this rejection be withdrawn.

ii. WO 96/12801 does not teach a promoter that is active in mammalian cells and, therefore, the present claims are not anticipated

Claims 1-10, 13-41, and 44-62 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 96/12801 (the priority document for U.S. Patent No. 6,395,964).

The content of WO 96/12801 and Arntzen, *supra* is very similar. Applicants contend that WO 96/12801 discloses only plant-expressible promoters and not a mammalian promoter as presently recited. For these reasons and the reasons related in the preceding subsection, Applicants believe that WO 96/12801 does not teach each and every element of claim 1 and that, therefore, it does not anticipate the subject matter of claims 1-10, 13-41, and 44-62. Accordingly, Applicants respectfully request that this rejection be withdrawn.

iii. Neither U.S. Patent Nos. 5,770,203 nor 5,874,287 teach nucleic acids coated onto a core carrier and, therefore, the claimed invention is not anticipated

Claims 1, 6-9, 11-18, 20, 22-24, 30-31, 32, 37-40, 42-49, 51, 53-55, 61-62 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,770,203 or under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,874,287.

The Examiner states that the disclosures of the '203 and the '287 patents (collectively, "Burnette") "are identical but evidence differing issue dates and claimed inventions." Office Action at page 10.

Neither of the two Burnette references discloses a composition comprising nucleic acid sequences that are coated onto a core carrier as recited in claim 1. Burnette is concerned with peptide vaccines and nucleic acid constructs for producing those peptide vaccines. The nucleic acid constructs are not coated onto core carriers because the constructs are not intended for administration to a subject and, particularly, are not intended to be delivered transdermally using a particle delivery device. Instead, Burnette's constructs are transformed into *E. coli* to produce the desired peptides. See column 9, line 5 and column 15, line 5 of the '203 patent and column 9, line 15 and column 15, lines 1 and 2 of the '287 patent.

Since neither the '203 patent nor the '287 patent disclose each and every element of the present claims, Applicants contend that claims 1, 6-9, 11-18, 20, 22-24, 30-31, 32, 37-40, 42-49, 51,

53-55, 61-62 are not anticipated. Accordingly, Applicants respectfully request that this rejection be withdrawn.

iv. WO 97/02348 does not teach nucleic acids coated onto a core carrier and, therefore, the claimed invention is not anticipated

Claims 1-10, 14, 22-24, and 30-31 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 97/02348.

The Examiner alleges that WO 97/02348 discloses "the instantly claimed invention directed to compositions that comprise first and second nucleic acid sequences." Office Action at page 12.

Applicants contend that WO 97/02348 does not teach nucleic acids coated onto a core carrier. Since WO 97/02348 does not disclose each and every element of claims 1-10, 14, 22-24, and 30-31, these claims are not anticipated by WO 97/02348. Accordingly, Applicants respectfully request that this rejection be withdrawn.

VII. Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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Amendments to the Drawings:

The replacement drawing sheets attached in connection with the above-identified application containing Figure(s) 1-1 to 14 are being presented as a new formal sheets to be substituted for the previously submitted drawing sheet or sheets. The only changes that have been made to the drawings is the removal of the 1/23, 2/23, 3/23, 4/23 . . . *etc.* page identifier from the top of each page.